

REMARKS

The Applicant hereby submits the present Amendment and Request for Reconsideration, entry of which is earnestly solicited. Claims 1, 3-4, 15, 17-18, 29-32, 34-39, 41-43, and 45 have been amended; claims 2, 5-14, 16, 19-28, 33, 40, and 44 have not been amended; no claims have been added or canceled. Thus, claims 1-45 are still pending in the application. By amending the above-referenced claims, the Applicant respectfully submits that no new matter has been added.

In the Office Action mailed on December 4th 2003, the Examiner rejected claims 1-45 under 35 U.S.C. Sect. 102 and 103 based on U.S. Patent No. 6,007,231, U.S. Patent No. 5,814,491, U.S. Patent No. 6,470,277, U.S. Patent No. 5,807,681, and U.S. Patent No. 6,475,736, U.S. Patent No. 6,401,043. In response, the Applicant respectfully submit that the claims are allowable for the following reasons.

First, the Applicant amends claims 1, 15, and 43 with the following limitation which is not taught nor suggested in the prior art alone or in combination:

the set of primer selection rules including a rule specifying that no primer pair data be identified for that which is found within prestored gene family data associated with the gene sequence

Such unique primer selection rules of the present application provide for an efficient high-speed high-throughput processing of gene sequence data along with a reduction of discrepancies that are not real polymorphisms or "false SNPs". Detailed features and advantages for the primer selection rule limitation are described in the present application on pp. 32-41. For example:

Without this functionality, primers that would amplify three different regions at the same time would be designed: the topo2a region of interest; the topo2b region related to it; and a nuisance region in chromosome 18. Unfortunately, the resulting data would show numerous discrepancies that are not real polymorphisms. These sequences are actually from different genetic positions that are highly similar to one another but not identical. Thus, most of the "SNPs" found in this manner are not SNPs at all. If one tried to genotype people at a "false SNP," they would get incoherent data as they would be looking at three different positions within the genome at the same time. It is important to produce data for single positions at a time so that the data can be accurately read and interpreted. (See pp. 41-42 of the present application.)

Other arguments can clearly be made for the further allowance of claims 1, 15, and 43, as well as claims which depend from them, but are moot in light of the above described reason for allowance of the claims.

Second, the Applicant amends claims 29 and 36 with some of the following limitations which are not taught nor suggested in the prior art of record alone or in combination:

comparing, by the computer, the nucleotide base quality information with predetermined qualification data which is based on end-user input data

based on the nucleotide base quality information meeting the predetermined qualification data: causing, by the computer, the nucleotide base position and aligned nucleotide base identifiers at the nucleotide base position to be visually displayed

along with a visual prompt for end-user acceptance or rejection

Such unique inspection and analysis processes of the present application again provide for an efficient high-speed high-throughput processing of gene sequence data along with a reduction of discrepancies that are not real polymorphisms or "false SNPs". Detailed features and advantages for the inspection and analysis processes are described in the present application on pp. 43-55. For example:

DNA sequences from various individuals are aligned using a conventional sequence alignment algorithm (at step 320), such as that provided using conventional Clustal software functions available by and from the EMBL, Heidelberg Germany, and is a re-write of the popular Clustal V program described by Higgins, Bleasby, and Fuchs (1991) CABIOS, 8, 189-191 (Thompson, J.D., Higgins, D.G. and Gibson, T.J. (1994) (CLUSTAL W: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, positions-specific gap penalties and weight matrix choice. Nucleic Acids Research, 22:4673-4680). Thus, the sequence alignment file is the first input file to the program. Any discrepancy that occurs within a neighborhood of other discrepancies is recognized so that the quality value information can be checked. If this information is greater than predetermined quality information, such as a user-defined input value, it is accepted and presented to the user for final acceptance. If not, it is discarded. The quality control file created from the phred functionality serves as the second input file.

In the sequence within which the discrepancy occurs, positions of the minor letters of the discrepancy are presented to the end-user. This lets the end-user contemporaneously call up the raw DNA sequence chromatogram and find the actual trace data peak for

the letter. This is advantageous because a visual inspection of raw DNA sequence data is the most reliable method of determining whether a discrepancy is valid. While the purpose of the software is to eliminate many time consuming steps, in some cases, borderline quality values nonetheless necessitate its execution. The presentation of the precise position and relevant file names for a discrepancy makes this step easy to execute. Also, the end-user is shown presentations of discrepancies that do not meet the quality control criteria. This is important because, in some cases, a borderline quality value may conceal good data due to other problems with sequence compressions or peak spacing. *(See pp. 44-45 of the present application.)*

Other arguments can clearly be made for the further allowance of claims 29 and 36, as well as claims which depend from them, but are moot in light of the above described reason for allowance of the claims.

Claims dependent from claims 29 and 36 have further limitations not taught or suggested in the prior art of record alone or in combination, such as:

based on the nucleotide base quality information meeting the predetermined qualification data: causing, at the computer, a viewing of a sequence chromatogram trace at the nucleotide base position *(see claims 30 and 37, and page 44 of the present application, for example)*

based on the nucleotide base quality information meeting the predetermined qualification data: causing neighboring aligned nucleotide base identifiers to be visually displayed along with the aligned nucleotide base identifiers at the nucleotide base position *(see claims 34 and 41, and page 54 of the present application, for example)*

wherein the one or more phred-based values comprise one or more average phred values calculated by the computer based on an average of a plurality of phred values associated with the aligned nucleotide base identifiers at the nucleotide base position where the difference exists (*see claims 35 and 42, and page 47-48 of the present application, for example*)

Thank you for your consideration. Please feel free to contact the undersigned for any reason if it would expedite the prosecution of the present application.

Respectfully Submitted,

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